General

Guideline Title

Prenatal screening for fetal aneuploidy in singleton pregnancies.

Bibliographic Source(s)

Chitayat D, Langlois S, Wilson RD. Prenatal screening for fetal aneuploidy in singleton pregnancies. J Obstet Gynaecol Can. 2011 Jul;33(7):736-50. [106 references] PubMed

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Summers AM, Langlois S, Wyatt P, Wilson RD, Society of Obstetricians and Gynaecologists of Canada. Prenatal screening for fetal aneuploidy. J Obstet Gynaecol Can 2007 Feb;29(2):146-61.

Recommendations

Major Recommendations

The quality of evidence (I-III) and classification of recommendations (A-L) are defined at the end of the "Major Recommendations."

Invasive Prenatal Diagnosis to Be Limited to Women at Increased Risk of Fetal Aneuploidy

1. All pregnant women in Canada, regardless of age, should be offered, through an informed counselling process, the option of a prenatal screening test for the most common clinically significant fetal aneuploidies in addition to a second trimester ultrasound for dating, assessment of fetal anatomy, and detection of multiples. (I-A)
2. Counselling must be non-directive and must respect a woman's right to accept or decline any or all of the testing or options offered at any point in the process. (III-A)
3. Maternal age alone is a poor minimum standard for prenatal screening for aneuploidy, and it should not be used a basis for recommending invasive testing when non-invasive prenatal screening for aneuploidy is available. (II-2A)
4. Invasive prenatal diagnosis for cytogenetic analysis should not be performed without multiple marker screening results except for women who are at increased risk of fetal aneuploidy (a) because of ultrasound findings, (b) because the pregnancy was conceived by in vitro fertilization with intracytoplasmic sperm injection, or (c) because the woman or her partner has a history of a previous child or fetus with a chromosomal abnormality or is a carrier of a chromosome rearrangement that increases the risk of having a fetus with a chromosomal abnormality. (II-2E)

Choosing a Screen

5. At minimum, any prenatal screen offered to Canadian women who present for care in the first trimester should have a detection rate of 75% with no more than a 3% false-positive rate. The performance of the screen should be substantiated by annual audit. (III-B)
6. The minimum standard for women presenting in the second trimester should be a screen that has a detection rate of 75% with no more than a 5% false-positive rate. The performance of the screen should be substantiated by annual audit. (III-B)

Review of Screening Options

First Trimester Screening: Nuchal Translucency Combined with Biochemical Markers

7. First trimester nuchal translucency should be interpreted for risk assessment only when measured by sonographers or sonologists trained and accredited for this service and when there is ongoing quality assurance (II-2A), and it should not be offered as a screen without biochemical markers in singleton pregnancies. (I-E)
8. Evaluation of the fetal nasal bone in the first trimester should not be incorporated as a screen unless it is performed by sonographers or sonologists trained and accredited for this service and there is ongoing quality assurance. (II-2E)
9. For women who undertake first trimester screening, second trimester serum alpha fetoprotein screening and/or ultrasound examination is recommended to screen for open neural tube defects. (II-1A)

Serum Integrated Prenatal Screening

10. Timely referral and access is critical for women and should be facilitated to ensure women are able to undergo the type of screening test they have chosen as first trimester screening. The first steps of integrated screening (with or without nuchal translucency), contingent, or sequential screening are performed in an early and relatively narrow time window. (II-1A)
11. Ultrasound dating should be performed if menstrual or conception dating is unreliable. For any abnormal serum screen calculated on the basis of menstrual dating, an ultrasound should be done to confirm gestational age. (II-1A)

The Use of Ultrasound in Screening for Chromosomal Anomalies

12. The presence or absence of soft markers or anomalies in the 18- to 20-week ultrasound can be used to modify the a priori risk of aneuploidy established by age or prior screening. (II-2B)

Factors Potentially Affecting Screening Performance

13. Information such as gestational dating, maternal weight, ethnicity, insulin-dependent diabetes mellitus, and use of assisted reproduction technologies should be provided to the laboratory to improve accuracy of testing. (II-2A)

General Considerations

14. Health care providers should be aware of the screening modalities available in their province or territory. (III-B)
15. A reliable system needs to be in place ensuring timely reporting of results. (III-C)
16. Screening programs should be implemented with resources that support audited screening and diagnostic laboratory services, ultrasound, genetic counselling services, patient and health care provider education, and high quality diagnostic testing, as well as resources for administration, annual clinical audit, and data management. In addition, there must be the flexibility and funding to adjust the program to new technology and protocols. (II-3B)

Definitions:

Quality of Evidence Assessment*

I: Evidence obtained from at least one properly randomized controlled trial

II-1: Evidence from well-designed controlled trials without randomization

II-2: Evidence from well–designed cohort (prospective or retrospective) or case–control studies, preferably from more than one centre or research group

II-3: Evidence obtained from comparisons between times or places with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of treatment with penicillin in the 1940s) could also be included in this category.

III: Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees

*Adapted from the Evaluation of Evidence criteria described in the Canadian Task Force on Preventive Health Care.

Classification of Recommendations†

A. There is good evidence to recommend the clinical preventive action.

B. There is fair evidence to recommend the clinical preventive action.

C. The existing evidence is conflicting and does not allow to make a recommendation for or against use of the clinical preventive action; however, other factors may influence decision-making.

D. There is fair evidence to recommend against the clinical preventive action.

E. There is good evidence to recommend against the clinical preventive action.

L. There is insufficient evidence (in quantity or quality) to make a recommendation; however, other factors may influence decision-making.

†Adapted from the Classification of Recommendations criteria described in the Canadian Task Force on Preventive Health Care.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

- Fetal aneuploidy (e.g., Down syndrome and trisomy 18)
- Singleton pregnancy

Guideline Category

Counseling

Risk Assessment

Screening

Clinical Specialty

Medical Genetics

Obstetrics and Gynecology

Radiology

Intended Users

Advanced Practice Nurses

Physician Assistants

Physicians

Guideline Objective(s)

To develop a Canadian consensus document on maternal screening for fetal aneuploidy (e.g., Down syndrome and trisomy 18) in singleton pregnancies

Target Population

All pregnant women in Canada

Interventions and Practices Considered

1. Offering noninvasive prenatal screening for fetal aneuploidy to all pregnant women, regardless of age
2. Offering invasive prenatal diagnosis only to women at increased risk of fetal aneuploidy
3. Screening options:
    - First-trimester screen (nuchal translucency combined with biochemical markers)
    - Second-trimester screen
    - Two-step screens (contingent, integrated, serum integrated, sequential)
4. Use of ultrasound in screening

Major Outcomes Considered

Performance of screening options in relation to:

- Detection rate or sensitivity
- False-positive rate
- Positive rate
- Positive predictive value

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Searches of Electronic Databases

Searches of Unpublished Data

Description of Methods Used to Collect/Select the Evidence

Studies published between 1982 and 2009 were retrieved through searches of PubMed or Medline and CINAHL and the Cochrane Library, using appropriate controlled vocabulary and key words (aneuploidy, Down syndrome, trisomy, prenatal screening, genetic health risk, genetic health surveillance, prenatal diagnosis). Results were restricted to systematic reviews, randomized controlled trials, and relevant observational studies. There were no language restrictions. Searches were updated on a regular basis and incorporated in the guideline to August 2010. Grey (unpublished) literature was identified through searching the websites of health technology assessment and health technology assessment-related agencies, clinical practice guideline collections, clinical trial registries, and national and international medical specialty societies. The previous Society of Obstetricians and Gynaecologists of Canada guidelines regarding prenatal screening were also reviewed in developing this clinical practice guideline.

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Quality of Evidence Assessment*

I: Evidence obtained from at least one properly randomized controlled trial

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III: Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees

*Adapted from the Evaluation of Evidence criteria described in the Canadian Task Force on Preventive Health Care.

Methods Used to Analyze the Evidence

Systematic Review

Description of the Methods Used to Analyze the Evidence

The quality of evidence was rated using the criteria described in the Report of the Canadian Task Force on Preventive Health Care (see the "Rating Scheme for the Strength of the Evidence" field).

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Not stated

Rating Scheme for the Strength of the Recommendations

Classification of Recommendations†

A. There is good evidence to recommend the clinical preventive action.

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C. The existing evidence is conflicting and does not allow to make a recommendation for or against use of the clinical preventive action; however, other factors may influence decision-making.

D. There is fair evidence to recommend against the clinical preventive action.

E. There is good evidence to recommend against the clinical preventive action.

L. There is insufficient evidence (in quantity or quality) to make a recommendation; however, other factors may influence decision-making.

†Adapted from the Classification of Recommendations criteria described in the Canadian Task Force on Preventive Health Care.

Cost Analysis

Generally, the costs associated with screening are measured by the cost per Down syndrome pregnancy diagnosed. This has been estimated using different screening options in several published studies. One of the difficulties with cost analyses is that the expenses associated with the ultrasound and serum sample analyses vary greatly from one jurisdiction to another. In addition, cost has not been estimated for many screening options, including the second trimester ultrasound. Consequently, a comprehensive cost comparison remains to be undertaken.

A published study of computer simulations to compare integrated, sequential, and contingent screening strategies with various cut-offs leading to 19 potential screening algorithms showed that the contingent screening strategy had the best cost-effectiveness ratio, with fewer procedure-related euploid miscarriages and unnecessary terminations.

It is not possible at this time to undertake a detailed cost-benefit analysis of the implementation of this guideline, since this would require health surveillance and research and health resources not presently available; however, these factors need to be evaluated in a prospective approach by provincial and territorial initiatives.

Method of Guideline Validation

Internal Peer Review

Description of Method of Guideline Validation

This clinical practice guideline has been prepared by the Genetics Committee of the Society of Obstetricians and Gynaecologists of Canada (SOGC) and the Prenatal Diagnosis Committee of the Canadian College of Medical Geneticists (CCMG). It was approved by both the Executive and Council of the Society of Obstetricians and Gynaecologists of Canada and the Board of Directors of the Canadian College of Medical Geneticists.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

- Reduction of the number of prenatal invasive procedures done when maternal age is the only indication
- Reduction of the numbers of normal pregnancies lost because of complications of invasive procedures
- Availability of prenatal screening to all pregnant women and early detection of fetal aneuploidy (trisomy 13, 18, 21)

Potential Harms

Possible false positive rate, an inherent risk with any screening test, which may result in undue anxiety

Qualifying Statements

Qualifying Statements

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Implementation Tools

Foreign Language Translations

Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Staying Healthy

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

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Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2007 Feb (revised 2011 Jul)

Guideline Developer(s)

Canadian College of Medical Geneticists - Professional Association

Society of Obstetricians and Gynaecologists of Canada - Medical Specialty Society

Source(s) of Funding

Society of Obstetricians and Gynaecologists of Canada

Guideline Committee

Society of Obstetricians and Gynaecologists of Canada Genetics Committee

Canadian College of Medical Geneticists Prenatal Diagnosis Committee

Composition of Group That Authored the Guideline

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Financial Disclosures/Conflicts of Interest

Disclosure statements have been received from all members of the committees.

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Guideline Availability

Electronic copies: Available in Portable Document Format (PDF) from the Society of Obstetricians and Gynaecologists of Canada (SOGC) Web site. Also available in French from the SOGC Web site.

Print copies: Available from the Society of Obstetricians and Gynaecologists of Canada, La société des obstétriciens et gynécologues du Canada

(SOGC) 780 promenade Echo Drive Ottawa, ON K1S 5R7 (Canada); Phone: 1-800-561-2416.

Availability of Companion Documents

A list of screening terminology is included in the Appendix of the original guideline document .

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI Institute on February 5, 2009. This summary was updated by ECRI Institute on October 19, 2011. The updated information was verified by the guideline developer on November 14, 2011.

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